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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/602,362	06/22/2000	Dirk Jager	LUD-5615.1-CIP-(10006411)	8875

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/602,362	JAGER ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89,101-105,113,132-134 and 158-165* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *89,101-105,113 and 132-134* is/are rejected.

7)☒ Claim(s) *158-165* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Re: Jager *et al.*

Dates of priority: 11/30/99 (SEQ ID NO:15)

06/22/2000 (SEQ ID NO:22, 26)

The election filed 05/17/2004 in response to the Office Action of 04/23/2004 is acknowledged and has been entered. Applicant has elected Group II, Claims 89, 101-105, 113, 132-134 without traverse.

Claims 158-165 were added.

Claims 89, 101-105, 113, 132-134, and 158-165 are currently under consideration.

Priority

A review of the parent application (09/451739) did not appear to reveal support for peptides encoded by SEQ ID NO:22 and 26. Thus, these sequences have priority only to the effective filing date of the current application-- 06/22/2000. If applicant disagrees with any rejection set forth in this office action based on the above priority date for SEQ ID NO:22 and 26, applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 103-104, 132-134 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the claim language in Claims 103 and 132 are vague as it is not clear what is encompassed by the claimed composition. For example, the immunogenic composition of Claim 103 comprises "at least one peptide consisting of an amino acid sequence of from 8 to 12 amino acids concatenated to each other in the isolated cancer associated cancer antigen of claim 89". So, at the very least, it would appear that the immunogenic composition comprises at least one peptide that is 8 amino acids long. But, what is the nexus between this peptide and the cancer antigen of Claim 89? It's not clear if these peptides are derived from the cancer antigens of Claim 89 or if they are in some type of mixture. Hence, the metes and bounds of the claims cannot be adequately determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 89, 101-105, 113, 132-134 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth an isolated cancer associated antigen or immunogenic composition thereof comprising (and or consisting) of the amino acid sequence encoded by SEQ ID NO:15, 22, or 26

and therefore the written description is not commensurate in scope with the claims which read on a large variety of allelic variants, fragments, and derivatives of amino acids encoded by SEQ ID NO. 15, 22, or 26.

The claims are drawn to isolated cancer associated antigens comprising all of the amino acid sequence encoded by SEQ ID NO. 15, 22, or 26, **or** at least 8 concatenated amino acids in the amino acid sequence encoded by SEQ ID NO:15, 22, or 26. The claims are further drawn to a composition of matter useful in treating a cancerous condition, comprising a peptide consisting of an amino acid sequence found in the amino acid sequence encoded by SEQ ID NO: 15, 22, or 26 or a composition comprising at least one peptide consisting of an amino acid sequence of from 8 to 12 or 8 to 25 amino acids concatenated to each other in the isolated cancer associated antigen of claim 89. Hence, the claims are broadly inclusive of a multitude of unrelated concatenated amino acids that do not possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, there are no significant identifying features in the claims. Further, there is no identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing

identifying characteristics, the specification does not provide an adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated cancer associated antigen or immunogenic composition thereof comprising (and or consisting) of the amino acid sequence encoded by SEQ ID NO:15, 22, or 26, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written

description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Additionally, Claim 113 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to a composition of matter useful in treating a cancerous condition comprising a peptide consisting of an amino acid sequence found in the amino acid sequence encoded by SEQ ID NO:15, 22, 26; an MHC or HLA molecule, and a pharmaceutically acceptable carrier.

However, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice and or use the invention commensurate in scope with the claims. The specification does not provide sufficient guidance and or objective evidence that such a composition would predictably be useful in treating a cancerous condition. For example, there is no teaching of administering (either in-vitro or in-

vivo) a pharmaceutical composition comprising an antigen encoded by either SEQ ID NO:15, 22, or 26 or fragment thereof that predictably treats a cancerous condition.

In general, the treatment of cancer is highly unpredictable as underscored by Gura (Science, v278, 1997, pp.1041-1042) who discusses the potential shortcomings of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice- particularly strains which have tumor suppressor gene knockouts, and problems of clonogenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041, 1st column) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive. Gura further teaches that very few drugs tested in xenografts models have made it to clinical practice and that attempts to use human cells in culture don't seem to be faring any better, partly because cell culture provides no information about whether a drug will make it to the tumor site (page 1041, 3rd paragraph). All of this underscores the criticality of providing workable examples which is not disclosed in the specification, particularly in an unpredictable art, such as cancer therapy. Moreover, Bellone et al. (Immunology Today, v20 (10), 1999, pp.457-462) summarize the state of the art of peptide immunotherapy including clinical trials where "there is usually a poor correlation between induction of specific T-cells and the clinical responses" (page 457, 2nd column) and further includes such disadvantages as (1) there is no direct evidence for a role in tumor rejection, (2) the therapy is applicable to few patients, (3) risk of generating tumor escape mutants, and (4) risk of autoimmune reactions (page 461, Box 1).

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the composition would function as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 89, 101-105, 132-134 are rejected under 35 U.S.C. 102(e) as being anticipated by Yuqiu *et al.* (US Patent No. 6,590,076; April 1999).

Yuqiu *et al.* teach an isolated cancer associated antigen comprising all or at least 8 concatenated amino acids in the amino acid sequence encoded by SEQ ID NO:15 (see attached sequence comparison). The reference further teaches immunogenic compositions comprising the antigen and a pharmaceutically acceptable adjuvant including cytokine adjuvants (see the claims and column 15, line 25). The patent further teaches (column 12, lines 55+) that the pharmaceutical compositions may comprise one or more polypeptides, each of which may contain one or more of the inventive sequences (or variants thereof), and a physiologically acceptable carrier or they may contain other epitopes of breast tumor antigens, either

incorporated into a combination polypeptide (i.e., a single polypeptide that contains multiple epitopes) or present within a separate polypeptide all of which read upon wherein the composition comprises a plurality of peptides which complex with a specific MHC molecule and or a plurality of MHC binding peptides.

Claims 89, 101-105, 132-134 are further rejected under 35 U.S.C. 102(e) as being anticipated by Yuqiu *et al.* (US Patent No. 6,579,973; November 1999).

Yuqiu *et al.* teach an isolated cancer associated antigen comprising all or at least 8 concatenated amino acids in the amino acid sequence encoded by SEQ ID NO:26 (see attached sequence comparison). The reference further teaches immunogenic compositions comprising the antigen and a pharmaceutically acceptable adjuvant including cytokine adjuvants (column 35). The patent further teaches (columns 25-26) that the immunogenic compositions may comprise additional portions and variants of the inventive sequences, and a physiologically acceptable carrier which encompasses wherein the composition comprises a plurality of peptides which complex with a specific MHC molecule and or a plurality of MHC binding peptides.

Claims 158-165 are objected as being dependent from a rejected base claim.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GBN
July 21, 2004